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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,595	03/16/2006	Koichiro Kano	8062-1033	7278
<small>465</small> YOUNG & THOMPSON 209 Madison Street Suite 500 ALEXANDRIA, VA 22314			<small>7590</small> EXAMINER POPA, ILEANA	
			<small>12/23/2008</small> ART UNIT 1633	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/560,595

Applicant(s)

KANO, KOICHIRO

Examiner

ILEANA POPA

Art Unit

1633

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 September 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15-34 is/are pending in the application.
- 4a) Of the above claim(s) 20-22, 26-28, 33 and 34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 15-19, 23-25 and 29-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☒ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

1. Claims 1-14 have been cancelled. Claims 20-22, 26-28, 33, and 34 have been withdrawn. Claims 15, 19, 24, 25, and 30-32 have been amended.

Claims 15-19, 23-25, and 29-32 are under examination.

Information Disclosure Statement

2. In the non-final Office action mailed on 06/10/2008, the Examiner indicated that the foreign references JP 2000-83656 and JP 2002-537849 disclosed on the IDS form of 12/13/2005 have not been considered because Applicant did not provide the documents.

Applicant argues that copies of the references should have been forwarded to the USPTO by the International Search Authority. Nonetheless, Applicant notes that an English translation of the foreign document JP 2002-537849 has been submitted with the reply filed on 09/10/2008.

In response Applicant's argument, it is noted that a copy of the foreign reference JP 2000-83656 has not been submitted to the USPTO by any of International Search Authority or Applicant. It is also noted that the foreign reference JP 2000-83656 is not in English and therefore, in order for the reference to be considered, an English translation is required.

Because Applicant provided an English translation of the foreign document JP 2002-537849, this document is hereby considered.

Priority

3. In the non-final Office action mailed on 06/10/2008, the Examiner indicated that, while a certified foreign priority paper has been received, Applicant did not provide an English translation of the foreign priority paper.

Applicant argues that, a verified English translation is only necessary to overcome intervening art, which is not the case here. Thus, Applicant argues, the requirement to establish foreign priority has been met.

Applicant's arguments are acknowledged however, without an English translation of the foreign priority document, the Examiner cannot establish whether the foreign priority document provides support for all embodiments recited in the claims. Therefore, the requirement to establish foreign priority has not been met.

However, since establishing priority will not overcome the art rejections of record, Applicant is not required to submit an English translation of the foreign priority document.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 15, 18, 23, and 24 remain rejected under 35 U.S.C. 102(b) as being anticipated by Park et al. (Bone, 1999, 24: 549-554), as evidenced by Lecoeur et al. (Biomaterials, 1997, 18: 989-993, Abstract).

Park et al. teach isolating, cultivating, and cloning mature adipocytes from human bone marrow; and the cloned mature adipocytes are further dedifferentiated to fibroblast-like fat cells (i.e., pre-adipocytes), wherein the pre-adipocytes express alkaline phosphatase, i.e., an early marker of osteogenesis (see Lecoeur et al., Abstract) (claim 15); Park et al. teach further transdifferentiating their pre-adipocytes into osteoblasts (claims 18, 23, and 24) (Abstract, p. 550, columns 1 and 2, p. 553, column 1, first full paragraph and column 2). Since Park et al. teach all claim limitations, the claimed invention is anticipated by the above-cited art.

Applicant traversed the instant rejection on the grounds that Park et al. do not disclose or suggest each and every element of the claimed invention. Specifically, Applicant argues that Park et al. do not teach inducing transdifferentiation of a preadipocyte cell line obtained by dedifferentiating a mature adipocyte. Applicant submits that the cell used for transformation in Park et al. is a fibroblast derived from brown adipocyte, which was differentiated from a bone marrow stromal cell. As such, Applicant argues, the fibroblast of Park et al. is different from the preadipocyte in the method of independent claim 15. Applicant argues that the cell obtained as an adipocyte by Park et al. was included in a suspended fraction obtained after centrifugation treatment of bone marrow samples. Therefore, according to Applicant, it

would have been necessary to first utilize collagenase processing and filtration by a mesh having pore size of approximately 250 μm in order to isolate an adipocyte from the suspended fraction. However, Park et al. does not carry out such steps. Consequently, it is believed that the cells used by PARK are isolated adipocytes, but a mixture of adipocytes and bone marrow stromal cells. Applicant notes that Park et al. appreciated that the cells present in the floating low-density layer of human bone marrow are mainly adipocytes and preadipocytes, wherein single adipocytes are present together with adipocytes associated in conglomerates with fibroblastic cells (p. 553). Applicant argues that the various stromal cells present in bone marrow tissue form clusters with adipocytes, and these clusters are likely to exist in the "cells contained in a suspended fraction after centrifugation of the bone marrow samples", which is the "adipocyte" of Park et al. However, Applicant argues, the prior art as evidenced by JP 2000-83656 in the IDS filed December 13, 2005, shows that in order to obtain a unilocular adipocyte, collagenase processing is needed, which includes multiple rounds of centrifugation and a filtration mesh of about 250 μm . Applicant argues that Park et al. fail to disclose or suggest any collagenase treatment and filtration. Applicant argues that Park et al. do not disclose checking the suspended fraction obtained to see if it is composed solely of adipocytes and therefore, the skilled artisan, upon reading Park et al., would understand that the cell in PARK is not a preadipocyte as required in claim 15. Applicant also argues that, in order to isolate the adipocytes contained in the reticular tissue of bone marrow to obtain a single fraction of adipocyte, it is necessary to digest the reticular fibers with collagenase and filter the

digested tissue to remove undigested tissue; centrifugation is used to force the adipocytes more to the upper layer fraction because lipid droplets abundant in the cytoplasm cause buoyancy while the other cells precipitate. Thus, Applicant argues, the pure adipocyte can be isolated. One skilled in the art at the time the invention was made was well aware that, if the enzyme digestion and filtration process is not followed, the adhesive cells recovered will contain various types of cells from the bone marrow tissue, and not the preadipocyte line as claimed. Additionally, Applicant argues that ceiling culture, as seen in the present application, enables floating adipocytes exclusively to be cultured; the obtaining of fibroblast-like adipocytes from the cell suspension containing only mature adipocytes is allegedly carried by Park et al. in side-well plates. One skilled in the art would be aware that it is impossible for the suspended cells to attach to the bottom of the wells because they remain suspended within the upper portion of the culture and medium due to the large amount of lipid droplets in cytoplasm. Accordingly, Applicant argues, the cell cluster containing adipocytes and bone marrow stromal cells, when cultured in six well culture dishes, is going to lead to fibroblasts falling off and there is doubt, therefore, as to the conclusions of Park et al. These fibroblasts from bone marrow stromal cells could be the ones which are subjected to later processing by Park et al. Applicant also argues that, in order to obtain the fibroblast-like cells, Park et al. used a culture medium in which the fraction was induced to differentiate into an adipocyte. However, a culture medium for inducing differentiation usually has the potential of maintaining the function of the adipocyte and suppressing dedifferentiation. Furthermore, Applicant asserts that there is no disclosure

that the cell line used in Park et al. expresses an early marker of osteogenesis, myogenesis or adipogenesis. One skilled in the art has read reports in a number of publications that, when using conventional preadipocyte strains, the early differentiation marker genes for adipogenesis are expressed only after induction of differentiation, but not before induction. One skilled in the art at the time of filing the application was of the opinion that the adipocyte maintained a function by .expressing adipocyte specific genes. Applicant submits that the absence of any mention of the early marker genes in Park et al. confirms that the identity of their cells remains unknown. Applicant submits that it is quite likely that the cells originated from the bone marrow stromal cells; bone marrow stromal cell populations contain pluripotent stem cells which could be induced to differentiate into adipocyte by the culture medium. Applicant further notes that Park et al. tried to prove that their cells were derived from adipocytes by using anti-AP2 antibody and Oil red O staining. The cells obtained by Park et al. expressed those markers because they had been cultured in a culture medium which induces the differentiation to adipocytes, i.e., these cells were the cells which had already been differentiated into adipocytes and possessed the function of adipocytes. In these differentiated cells, the expression of genes and proteins which are specifically expressed in other types of cells (bone, muscle and chondrocyte, for example) is suppressed. In order to differentiate into another cell type, the function of the adipocyte must be turned off by dedifferentiation. However, there appears to be no such measure taken for the cells obtained by Park et al. Thus, Applicant again submits that the cells obtained by Park must be different from the preadipocyte strain of the

method of claim 15 and are most likely derived from multi-locular adipocytes that have been induced by differentiation of bone marrow stromal cells that were contaminated during isolation. Therefore, Applicant requests the withdrawal of the rejection.

Applicant's arguments are acknowledged however, they are not found persuasive for the following reasons:

The instant claims are drawn to a method of transdifferentiating a preadipocyte cell line, wherein the preadipocyte cell line expresses markers of osteogenesis, myogenesis, or adipogenesis and wherein the preadipocyte cell line is obtained by dedifferentiating mature adipocytes. The claim does not recite any particular method for obtaining the mature adipocytes. Therefore, Applicant's argument that the claimed mature adipocyte is obtained by a method which is different from that used by Park et al. is irrelevant, because such is not recited in the claims; how one obtains the mature adipocytes has no bearing on the patentability of the claims. All that is required by the claims is to dedifferentiate mature adipocytes into preadipocytes, followed by the transdifferentiation of the preadipocytes into cells other than adipocytes. Park et al. teach isolating adipocytes from the floating fat layer obtained after the centrifugation of bone marrow cells and culturing them in adipocyte differentiation medium to maintain their differentiated state (i.e., Park et al. teach obtaining mature adipocytes); the mature adipocytes are cloned, dedifferentiated to preadipocytes, and transdifferentiated into osteogenic cells; the preadipocytes of Park et al. express osteogenic markers such as alkaline phosphatase (Abstract; p. 550, columns 1 and 2; p. 551, column 2, last paragraph; p. 552, columns 1 and 2; p. 553, column 1, first full paragraph, and column

2). Applicant argues that the cells of Park et al. expressed alkaline phosphatase because they are differentiated adipocytes. This argument is not found persuasive because Park et al. specifically teach that alkaline phosphatase is also expressed by their preadipocytes (see p. 551, column 2, last paragraph). Applicant also submits that it is quite likely that the cells of Park et al. originated from the contaminating bone marrow stromal cells. This is just an argument not supported by any evidence; "it is quite likely" does not equal evidence. In fact, Park et al. clearly teach that their mature adipocytes are not derived from bone marrow stromal cells (see p. 551, column 2, last paragraph; p. 553, column 1 bridging column 2, and column 2). Even assuming that the cells of Park et al. would be derived from bone marrow stromal cells, this in itself would not differentiate the claimed invention from the prior art because, as noted above, the claims do not require a specific method for obtaining the mature adipocytes to be dedifferentiated.

In conclusion, Park et al. teach a method of acquiring osteogenic cells (i.e., cells with other functions) by inducing the transdifferentiation of a preadipocyte cell line, wherein the preadipocyte cell line is obtained by dedifferentiating mature adipocytes derived from fat tissue and wherein the preadipocyte express osteogenic markers. In other words, Park et al. anticipate the invention of claims 15, 18, 23, and 24.

For the reasons set forth above, the rejection is maintained.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 15-18, 23, 24, 29, and 30 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al. taken with Lecoeur et al., in view of Sugihara et al. (Differentiation, 1986, 31: 42-49).

The teachings of Park et al. and Lecoeur et al. are applied as above for claims 15, 18, 23, and 24. Park et al. do not teach deriving their pre-adipocytes from the dedifferentiation of mature adipocytes isolated from subcutaneous fat tissue (claim 17). However, at the time the invention was made, deriving mature adipocytes from subcutaneous fat tissue and dedifferentiating them to fibroblast-like fat cells (i.e., pre-adipocytes) were both taught by the prior art. For example, Sugihara et al. teach a method of obtaining mature adipocytes from abdominal fat tissue, the method comprising chopping the tissue into small pieces, subjecting the chopped tissue to collagenase digestion followed by filtration and centrifugation, isolating the floating fat cells, followed by subjecting the isolated fat cells to "ceiling culture" to obtain pre-adipocytes (Abstract, p. 42, column 2, p. 44, column 1, second and third paragraphs, p. 45, column 1, p. 46, column 2). It would have been obvious to one of skill in the art, at the time the invention was made, to substitute the pre-adipocytes of Park et al. with those of Sugihara et al. to achieve the predictable result of transdifferentiating them into osteoblasts. Claim 14 recites that the preadipocyte cell line is FERM BP-0864, wherein

FERM BP-0864 cell line is obtained by the method of Sugihara et al. (see the instant specification, p. 8, 22, and 23). It is noted that Applicant did not provide any evidence that FERM BP-0864 cell line has unique properties as compared to other cell lines obtained by using the same method, i.e., the method of Sugihara et al. Absent evidence of unexpected results, it is generally not inventive to use the FERM BP-0864 cell line versus similar cell lines obtained by using the same method. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

8. Claims 15-19, 23-25, and 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al. taken with both Lecoeur et al. and Sugihara et al., in further view of each Ross et al. (Science, 2000, 289: 950-953), Bennett et al. (J Biol Chem, June 7, 2002, 277: 30998-31004), and Rando et al. (J Cell Biol, 1994, 125: 1275-1287).

Park et al., Lecoeur et al., and Sugihara et al. do not teach transdifferentiation to myoblasts (claims 19, 25, 31, and 32). However, at the time the invention was made, the prior art suggested that preadipocytes have the capability to transdifferentiate into myocytes. For example, Ross et al. teach that adipocytes and myocytes originate from the same precursor and that signaling by Wnt10b is required for commitment to the myocyte lineage; they also teach that inhibition of Wnt10b signaling in preadipocytes and myoblasts induces adipogenesis (Abstract, p. 952, columns 2 and 3). Bennett et al. teach that the Wnt10b receptors are highly expressed in preadipocytes and that inhibition of Wnt10b signaling leads to adipogenesis (Abstract, p. 30999, column 1, first

paragraph). Based on these teachings, one of skill in the art would have known that treating preadipocytes with a myoblast differentiation medium comprising Wnt10b would result in their transdifferentiation to myoblasts. It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Park et al., Lecoeur et al., and Sugihara et al. by transdifferentiating their preadipocytes to myoblasts, with a reasonable expectation of success. The motivation to do so is provided by Rando et al., who teach that myoblasts grown *in vitro* can regenerate muscle fibers when transplanted into a subject in need of treatment (Abstract, p. 1275, column 2, p. 1276, column 1). One of skill in the art would have been expected to have a reasonable expectation of success in doing so because the art teaches that preadipocytes express receptors for factors necessary for myoblast lineage commitment. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

Applicant traversed both obviousness type rejections above on the grounds that the cited prior art references fail to disclose or suggest inducing transdifferentiation of a preadipocyte cell line obtained by dedifferentiating a mature adipocyte. With respect to Park et al., Applicant's arguments are the same as above. Applicant submits that Lecoeur et al. and Sugihara et al. fail to remedy the deficiencies of Park et al. With respect to Sugihara et al., Applicant argues that the reference does not disclose preadipocytes which express an early marker, such as that of adipocyte (PPAR γ), bone cells (cbfa1) and myocytes (Myf5), whereas the preadipocytes of the present claims

already express those early markers. Thus, it is believed that the preadipocytes cell line of the present invention (FERM BP-0864) has unexpected properties compared to the cells of Sugihara et al. and such unexpected properties are indicative of the non-obviousness of the claims.

Additionally, Applicant argues that even assuming that one of ordinary skill in the art had a reasonable motivation in doing so because Ross et al. teach transforming preadipocytes to myoblasts, the skilled artisan would not have expected to transform preadipocytes into a few kinds of cells (including myoblasts) other than adipocytes. Please note the preadipocytes of the claims express not only an early marker of adipocytes and myoblast, but also an early marker of other cells. As such, even the skilled artisan would not reasonably arrive at the present invention based on the combined teachings of the references. Applicant notes that Ross et al. and Bennett et al. were relied upon as disclosing that adipocytes and myocytes originate from the same precursor and that signaling by Wnt10b is required for commitment to myocyte lineage and that inhibition of Wnt10b signaling leads to adipogenesis. However, Applicant argues, such teachings in no way describe or suggest inducing transdifferentiation of a preadipocyte cell line obtained by dedifferentiating a mature adipocyte as claimed. Thus, Applicant argues, Ross et al. and Bennett et al. fail to rectify the deficiencies of Park et al. Applicant argues that, although Rando et al. was relied upon as disclosing that myoblasts grown in vitro can regenerate muscle fibers when transplanted into subjects, Applicant fails to see how such disclosure allegedly provides motivation to modify the method of Park et al., Lecoecur et al., and Sugihara et al. by

transdifferentiating preadipocytes to myoblasts as noted by the Office. Further, Applicant argues, such teachings in no way describe or suggest inducing transdifferentiation of a preadipocyte cell line obtained by dedifferentiating a mature adipocyte as claimed. Therefore, Applicant submits that: (i) the cited references, taken alone or in combination, do not teach, suggest or otherwise make obvious the above-noted features of claim 15; and (2) the lack of clarity in Park et al. signifies that the combined references would not yield predictable results to arrive at the claimed method. For these reasons, Applicant argues, the cited references cannot render the claimed invention obvious and therefore, the rejections above should be withdrawn.

Applicant's arguments are acknowledged however, the rejection is maintained for the following reasons:

With respect to Park et al., see above. For the reasons set forth above, there is nothing to remedy in Park et al. and therefore, Applicant's argument that Lecoeur et al. and Sugihara et al. do not remedy the deficiencies of Park et al. is not found persuasive. With respect to Lecoeur et al., the reference was only cited as evidence that the alkaline phosphatase expressed by the preadipocytes of Park et al. is an early marker of osteogenesis (see above). Applicant argues that, since Sugihara et al. do not disclose preadipocytes which express an early marker, such as that of adipocytes (PPAR γ), bone cells (cbfa1) and myocytes (Myf5), the preadipocytes of the present invention (such as FERM BP-0864) express these early markers and therefore, they have unexpected properties. This argument is not found persuasive for the following reasons. First, the specification discloses that all preadipocyte obtained by the claimed

method (and not only FERM BP-0864 cells), express these markers (p. 8 and 9).

Second, the method of Sugihara et al. is identical to the claimed method (please compare p. 8, 9, 22, and 23 of the instant specification with p. 42 and Fig. 2 in Sugihara et al.) and therefore the cells of Sugihara et al. must necessarily express the markers above. Again, all that is required for PPAR γ , cbfa1, and Myf5 expression is to subject isolated unilocular fat cells to ceiling culture. Thus, the argument of unexpected properties is not found persuasive.

Applicant argues that the skilled artisan would not have expected to transform preadipocytes into cells types (including myoblasts) other than adipocytes. Such an argument is not found persuasive because the art teaches that preadipocytes can be transformed to other cell type, for example osteogenic cells (see the teachings of Park et al. above). Based on these teachings, one of skill in the art would have known that preadipocytes have the capability to transdifferentiate to cells other than adipocytes. Moreover, the prior art also suggested that preadipocytes have the capability to transdifferentiate into myocytes (see the teachings of Ross et al. and Bennett et al.). Specifically, the prior art teaches that: (i) both adipocytes and myocytes originate from preadipocytes; (ii) preadipocytes highly express receptors for Wnt10b; and (iii) signaling by Wnt10b is required for the commitment of preadipocytes to the myocyte lineage; inhibition of Wnt10b signaling in preadipocytes and myoblasts induces adipogenesis. Based on these teachings, one of skill in the art would have known that preadipocytes can transdifferentiate into myoblasts and would have reasonably expected to be successful in obtaining myoblasts from preadipocytes by growing the preadipocytes with

a medium comprising Wnt10b. Applicant argues that the teachings of Ross et al. and Bennett et al. do not describe or suggest inducing transdifferentiation of a preadipocyte cell line obtained by dedifferentiating a mature adipocyte as claimed. This argument is not found persuasive because the instant rejections are obviousness type rejections based on a combination of references, which combination teaches inducing transdifferentiation of a preadipocytes obtained by dedifferentiating mature adipocytes (see the rejection above).

With respect to Rando et al., the only argument provided is that Applicant fails to see how the reference provides the motivation to transdifferentiate preadipocytes to myoblasts. Failure to see is not enough for the argument to be persuasive. Just because Applicant fails to see it, does not mean that the reference does not provide the motivation. Applicant did not provide any explanation as to why Rando's teaching of using myoblasts grown *in vitro* to regenerate muscle fibers in subjects is not a motivation. This teaching in Rando et al., taken together with the ample teachings in the prior art of using stem or progenitor cells to generate differentiated cells *in vitro* for transplantation purposes, would motivate one of skill in the art to modify the method of Park et al., Lecoœur et al., and Sugihara et al. by transdifferentiating preadipocytes to myoblasts.

For the reasons set forth above, it is concluded that the combination of the cited references renders the claimed inventions *prima facie* obvious the above and the rejections are maintained.

Conclusion

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Voitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ileana Popa/
Examiner, Art Unit 1633